Reprinted from the 'Ophthalmological Society's Transactions,' Vol. XXXIII, 1913.

Fibrous tissue formation in connection with the fœtal vascular system and visible vessels on the surface of the iris.

By E. Treacher Collins.

(With Plates IX, X and XII, fig. 2.)

During part of fœtal life the lens vesicle is surrounded by a vascular sheath which attains its fullest development about the fourth month. The blood-vessels contained in this sheath are derived partly from the central hyaloid artery of the vitreous and partly from the anterior ciliary vessels at the limbus. The former divides into branches on the posterior surface of the lens which extend round its sides. The latter are situated in what has been termed the "anterior fibro-vascular sheath of the lens," or "pupillary membrane," but is more aptly described as

the *lamina irido-pupillaris*, because the vessels extend over the anterior surface of the iris, as well as across the pupil and the anterior surface of the lens.

This lamina irido-pupillaris is formed from the posterior part of the mesoblast which extends in between the lens vesicle and the surface epithelium, and from which the cornea is developed. Normally, it consists of little more than a plexus of vessels and spindle-shaped cells.

The iris is developed beneath this lamina by the extension inwards of the two layers of the secondary optic vesicle, or optic cup, with some mesoblast external to it. The two layers of the optic vesicle form the two layers of pigment epithelium on the posterior surface of the iris, and from the mesoblast external to them is derived its stroma, probably assisted in its development by the vascular lamina irido-pupillaris overlying it. This membrane, whilst it exists, has a system of blood-vessels distinct from those ultimately supplying the iris, which are situated deeper in its tissue.

The posterior part of the vascular sheath of the lens is continued forward round its sides and joins the lamina irido-pupillaris; in doing so, it has to pass round the internal edge of the advancing secondary optic vesicle.

Before birth the entire vascular sheath of the lens and the lamina irido-pupillaris disappear. Persistence of portions of it as delicate avascular strands are amongst the commonest of the congenital abnormalities of the eye which are met with. They may exist as delicate remnants of the central hyaloid artery attached to the posterior surface of the lens, or as fibres of pupillary membrane extending from the small circle of the iris into the pupillary area, or as an irregular network of light-coloured markings on the surface of the iris, most marked usually in the region of the small circle.

A much rarer form of congenital malformation is for this same fœtal vascular system, instead of persisting simply as delicate fibres to become transformed into dense cords or layers of fibrous tissue. Such formations of fibrous

tissue are most frequently met with in connection with the central hyaloid artery of the vitreous, either as a dense layer at the posterior surface of the lens, as one or more white cords extending forwards through the vitreous from the region of the optic disc, or as a spur projecting upwards into the vitreous from the region of fœtal ocular cleft. In these masses or columns of fibrous tissue, blood-vessels, patent and carrying blood, are usually present. It has been customary to speak of such formations as "atypical development of the vitreous humour."

The general opinion of embryologists seems now to be that the vitreous humour is not mesoblastic but epiblastic in origin. Salzmann (1), writing on this matter, says: "The views of embryologists have undergone a significant change in the last decades with respect to the genesis of the vitreous. Previously the vitreous was held to be a mesodermal structure. Now, with a few exceptions, the trend of the views is that the mesoderm forms only the vitreous vessels, that, however, the framework of the vitreous is of ectodermal origin. In respect to the finer details the views are still very much at variance; I, myself, have mainly followed the more intermediate views of Kölliker, von Szily, and Wolfrum." In a recent and lengthy investigation on the subject by Mawas and Magitot (2) the ectodermic origin of the vitreous body is also arrived at.

The blood-vessels, which grow in at the fœtal cleft, appear then only to supply nutriment to the developing vitreous, much as they supply nutriment to the developing lens during its most active period of growth.

A formation of fibrous tissue in connection with these vessels cannot any longer be strictly described as "atypical development of the vitreous"; it will be better to speak of it in future as atypical development of the fœtal vascular system.

That this is the correct way to regard it is, moreover, shown by the fact that formation of fibrous tissue of this description is not always confined to the vitreous chamber,

but may be met with in connection with other portions of the fœtal vascular system, *viz.*, with the extension forwards of the posterior part of the vascular sheath of the lens round its sides, and in connection with the lamina irido-pupillaris.

Hess (3), in a microphthalmic eye, described the extension of the formation of fibrous tissue at the posterior surface of the lens, in connection with a persistent hyaloid artery, round one side of the lens to the cornea, and attributed the coloboma of the iris present in that case to it.

Coats (4) has more recently brought forward confirmatory evidence of this hypothesis of Hess: that defects in development of the iris are due to toughened portions of the lateral extensions forward of the posterior fibro-vascular sheath checking its growth inwards. He also points out that a similar defect in the sheath might account for coloboma of the lens, or ectopia of the lens, by causing a defect in the development of the suspensory ligament.

In the description of the microscopical appearances of a congenital malformed eye Coats further speaks of the formation of a "fibrous membrane on the iris." The following is a quotation from his account of it in his Hunterian Lecture:

"In the microscopical description I spoke of a long-meshed membrane lying on the anterior surface of the iris, and continuous on the one hand with the loose tissue in the corneo-iridic angle, and on the other with the pupillary membrane; it frequently adheres to the iris stroma, but is, on the whole, a distinguishable structure. It is probably formed when the optic vesicle and the adjacent deep layers of the mesoblast grow in to form the iris by the persistence of some of the superficial mesoblastic layers which do not take part in the formation of the iris stroma. Should this membrane persist it is possible that it gives rise to a very rare abnormality in which a crescentic sheet of bluish-white fibrous tissue with a tendinous sheen covers part of the anterior surface of

the iris. The membrane may partially cover the pupil, which is displaced towards the side on which it occurs; the part of the pupil which is uncovered may react vigorously. So far as I know the only case in literature is one shown at the Ophthalmological Society by Mr. Sydney Stephenson (5), who well describes the appearances as follows: 'The impression conveyed to my mind is that it (the membrane) overlies the iris, and that if it could be removed iris tissue would be found behind it. A point in favour of this assumption is that at the extreme periphery a narrow zone of what seems to be iris can be recognised.' An exactly similar case was shown me once at Moorfields by Mr. W. T. Holmes Spicer."

I am quite familiar with the clinical appearances described in the above passage, but had never been able to offer any adequate explanation to account for them. Coats's suggestion that there is a persistence and fibrous thickening of the iridic portion of the lamina irido-pupillaris I think must be correct.

The best example of the condition which I have seen was a case shown before this Society by Marcus Gunn (6) in 1889, and published in its *Transactions* with an excellent illustration.

In connection with Coats's theory, the case is of special interest in that, besides the membrane on the surface of the iris, there were other malformations attributable to atypical fibrous thickening of the fœtal vascular system.

Marcus Gunn's description of the appearance of the iris is as follows: "The iris of the left eye is of a dark brown colour similar to that of the right eye, but exhibits apparent separation between the sphincter portion and the outer two thirds. The sphincter part is altogether on a posterior level to the rest of the iris, especially below, where it is both deep and displaced downwards, so as to be here in great measure concealed by the outer part of the iris. Doubtless there is a connection hidden from view, probably consisting of vertical or sloping bands of connective tissue, between the extreme outer part of the

sphincter portion and the inner part of the dilator portion, but the movements of the pupil on exposure to light and on the use of weak mydriatics are entirely confined to the inner third, and there is no manifest dragging on the outer two thirds on contraction to light."

In each of these eyes there was an ectopia and coloboma of the lens and a gap in the suspensory ligament of the lens. Gunn states that as the result of ophthalmoscopic examination he found "passing backwards from the blending of the lobules in the lens is a thick opaque cord, which traverses the vitreous to a point a little above the optic disc."

I have sections of a congenitally malformed eye showing thickening and persistence of a piece of the iridic part of the lamina irido-pupillaris.

The patient from whom the eye was removed was a female infant, who first came under the care of Mr. Lawford at Moorfields Hospital in November, 1893, when she was about four weeks old. Her right, the affected, eye had been considered larger than its fellow since birth, and "a spot" had been noticed on it two days. On examination the eye was found to be distended. The cornea was clear. The anterior chamber shallow, more so on the outer than the inner side. The pupil was active to light, slightly excentric, being displaced outwards, and pear-shaped. No note was made of any abnormal appearance of the iris. The lens was partly opaque and displaced outwards. Behind the lens, seen through the gap at the nasal margin, was an opaque, solid-looking pinkish mass with vessels in it.

The condition was thought possibly to be glioma of the retina, and the eye was excised a month after the infant's first visit to the hospital.

Pathological examination. — After the eyeball was hardened and opened by an antero-posterior horizontal section it showed: The anterior chamber very shallow, the iris apparently in contact with the cornea on the outer side. The lens small and displaced outwards with

PLATE IX.

Illustrates Mr. E. Treacher Collins's paper on Fibrous Tissue Formation in Connection with the Fœtal Vascular System and Visible Vessels on the Surface of the Iris (p. 173).

Figs. 1 and 2 show the difference in the appearance of the iris on the two sides of a section through the anterior half of the eyeball in the case recorded on p. 178.

In fig. 1, shows persistence of thickening of a portion of the iridic part of the fœtal lamina irido-pupillaris on the anterior surface of the iris.

In fig. 2, no such thickening is present, only a slight undue prominence of the anterior surface in the region of the small circle.

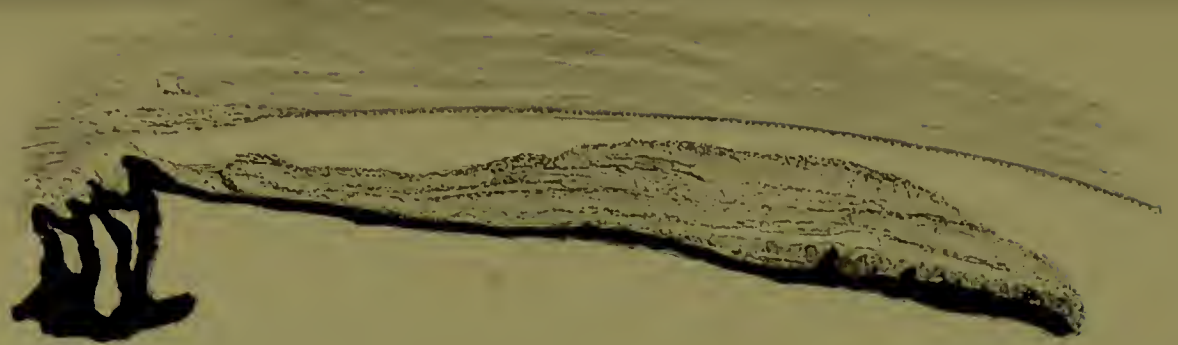
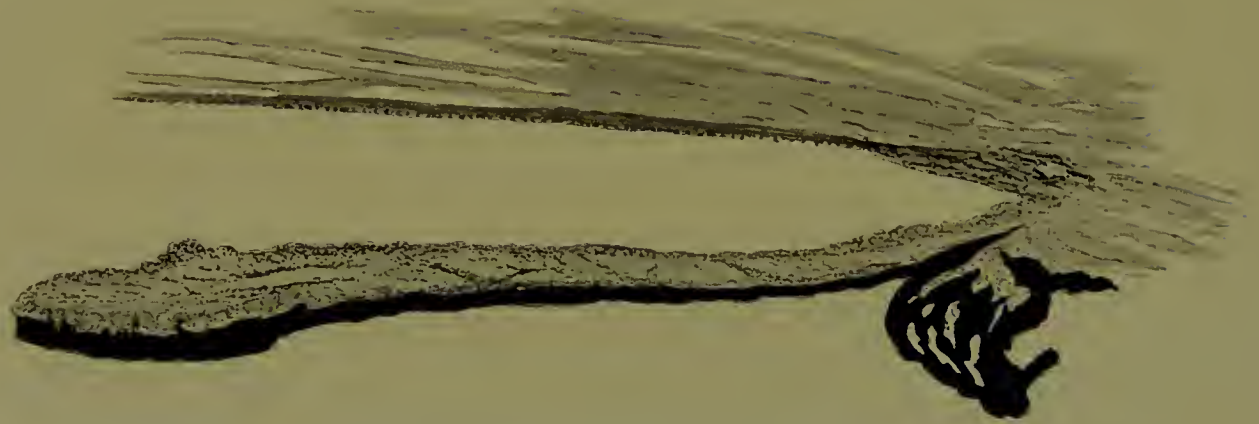


FIG. 2.



E. Treacher Collins, *del*.

Adlard & Son, Impr.

its nucleus sharply defined from the cortex and eccentric in position, being nearer the outer part of the capsule than the inner. Behind the lens, stretching across the ciliary region, was a white membrane about 1 mm. thick. Passing back from this membrane through the vitreous chamber to the posterior part of the eye were three cord-like bands, two large ones and one small one. On the inner surface of the lower and inner part of the globe extending from the optic disc to the equator was a thick white mass of firm consistency. Microscopical examination showed the bands stretching through the vitreous chamber, the white mass at its lower and inner part and the membrane behind the lens to consist of tissue of similar structure. It was composed of a condensed network of fibres and cells with elongated nuclei. Coursing through it were blood-vessels, which were seen cut in various directions and containing collections of red blood-corpuscles.

The iris on the two sides of a section through the anterior part of the globe presented a very different appearance. On the side towards which the lens was displaced it showed a normal condition except for a slight thickening on the surface in the region of the small circle (Pl. IX, fig. 2). On the opposite side, on the surface of the iris, was a cellular thickening, or membrane, which could be distinctly differentiated from the normal surface of the iris (Pl. IX, fig. 1). In the section in which it was most extensive, it extended from about the position of the small circle of the iris up to within a short distance of its root. It was seen to contain blood-vessels with red blood-corpuscles in them. The specimen was not cut in serial sections, and from those which have been preserved it is not possible to say with what other vessels those in this superficial membrane communicated.

That the pupillary portion of the lamina irido-pupillaris may in rare instances become developed into fibrous tissue is well shown in an illustration published in Greeff's (7) book on the pathological anatomy of the eye. In

this illustration, starting from the small circle of the iris, which is represented as a much thickened crenated line, are seen thick cord-like bands, which form a network over the pupil.

In cases where there is fibrous tissue development in connection with the central hyaloid artery, that vessel is very frequently patent with blood circulating in it. Whether when the anterior portion of the fœtal vascular system undergoes this unusual fibrous thickening some of the blood-vessels also persist, I do not know. Sometimes the vessels of the lamina irido-pupillaris may persist with blood circulating in them without any fibrous thickening, and can then be seen clinically as vessels on the surface of the iris. In 1907 I showed before this Society the sections of an eye of a cat, in which a portion of the lamina pupillaris had persisted and extended from the small circle of the iris to the posterior surface of the cornea to which it was attached. Blood-vessels could be seen carrying blood coursing forwards from the surface of the iris along these tags of membrane, and their presence was subsequently demonstrated by microscopical examination.

I have now to bring before you the drawing of the right eye of an infant, æt. 8 months, who came first under my observation at Moorfields Hospital about six months ago. The affected eye was somewhat smaller than its fellow, and a white spot had been noticed in it by the child's mother since birth. There was no history of any ophthalmia neonatorum.

On oblique illumination the lens was seen to be cataractous, of a greyish-white colour. It was apparently displaced somewhat inwards, for, in the extreme outer part of the pupillary area, there was a dark reflex.

The iris presented the usual slaty-blue colour of an infant's eye. Coursing over its surface and starting from the ciliary margin could be seen three blood-vessels as red lines. Two proceeded from below upwards, passed over the pupillary border, and broke up into branches on

the surface of the opaque lens. The third proceeded from the nasal side, and after passing the pupillary border, curled backwards round it, disappearing from view behind the iris (Pl. XII, fig. 2). The margin of the pupil was regular and circular, and, except for the blood-vessels, had no connection with the opaque lens.

There can be little doubt, I think, that the blood-vessel which curls round the border of the pupil represents the extension forwards of a branch of the central hyaloid of the vitreous, which normally, in fœtal life, effects a junction with the vessels of the lamina irido-pupillaris. In this eye, which was somewhat microphthalmic, the central hyaloid artery had, in all probability, remained persistent and patent, and this vessel on the iris formed the vein by which the blood circulating in that artery escaped from the eye.

In many of the eyes with a persistent and patent central hyaloid artery which have been examined microscopically, some difficulty has been experienced in determining by what venous channel the blood circulating in it leaves the eye.

Greeves (8) has, however, in a microphthalmic eye with a coloboma of the iris and a persistent and patent hyaloid artery, been able to trace, by means of serial sections, the junction of several venous radicles from the mass behind the lens into a single vein. This was situated down and in, and passed forwards beneath the lower margin of the lens capsule to the anterior chamber. It then turned upwards and inwards, and finally joined the inner pillar of the coloboma at its pupillary margin.

Blood-vessels visible clinically on the surface of the iris sometimes make their appearance as a pathological condition. Such vessels are usually met with in eyes with increased tension, most frequently in glaucoma, secondary to thrombosis of the central retinal vein, though it is not in every case of this sort that they form. The presence of iritis does not seem essential to their development, though they may be associated with it.

A case in which such new-formed vessels were visible is recorded by Holmes Spicer (9) in the *Transactions* of this Society for 1902, with a pathological description of the eye by J. H. Parsons. The case is entitled: "Vessels of new formation on the anterior surface of the iris after prolonged use of eserine; cystic degeneration of the retina at the yellow spot; old thrombosis of retinal veins."

The patient was a woman, æt. 65 years, who, besides increase of tension and symptoms indicating thrombosis of the central retinal vein, had had iritis, resulting in complete annular synechia.

Spicer describes the condition of the iris as follows: "The iris was generally discoloured, and there were several large vessels running across it lying apparently quite on the surface of a bright crimson colour; they did not follow the lines of any normal vessels, as they ran straight across the chamber from one side to the other; some were above the pupil and some were below."

In his pathological report of this case Parsons describes the condition of the iris as follows: "The iris is irregular in thickness. The stroma consists of compact fibrous tissue with many round cells, especially near the surface. There are some very large vessels cut transversely. Some are in the adherent part of the iris, others nearer the pupil. These clearly run horizontally and were visible clinically. They are mostly near the anterior surface. The pigment-epithelium is very irregular, and has proliferated into the stroma in places. It also forms cysts in places by separation from stroma."

In commenting on this case the author writes: "The formation of the new vessels on the surface of the iris is a matter of interest, as they did not appear to have arisen from any of the natural vessels of the iris; their direction was across the anterior chamber from one side to the other. Their growth and development occurred while the eye was being treated with eserine, and they began to shrink after atropine was used. The well-known action

of eserine in producing dilatation of the vessels of the anterior part of the eye is probably in part responsible for their appearance."

I have quoted at length from this case of Spicer's and Parsons' because it illustrates well several of the special features in connection with these new-formed vessels on the surface of the iris to which I particularly wish to direct attention.

(*a*) The location of the vessels on the surface of the iris and not in the stroma.

(*b*) The direction in which they run, not radially from the ciliary to the pupillary margin, like the vessels in the stroma, but often at right-angles to them, or in the form of an irregular network.

Though it is possible that eserine may in some cases favour their formation, the following case shows that it is not essential. It also serves to show that the new vessels may be restricted to a portion of the surface of the iris and not extend all over it.

The patient, Mrs. R—, æt. 73 years, was sent to me in June, 1910, by Mr. W. W. Sinclair, of Ipswich, to whom I am indebted for the notes. She was first seen by him in April, 1909; her sight had then been failing for some months. She had glycosuria. On examination there were found peripheral striæ in the lenses and abundant floating opacities in the vitreous of both eyes. These latter increased in the left eye with corresponding failure of sight, and in July there appeared to be some retinal haemorrhages, though the condition of the vitreous made it difficult to be certain of their presence. After a motor tour in September her condition became worse. The right eye showed extensive posterior synechiæ from "quiet" iritis and she could only count fingers with it. In the left eye vision was $\frac{5}{24}$. The tension in each eye was full.

Pilocarpine drops were used but did not suit, causing pain and headache without lowering tension. Since then atropin had been applied occasionally with benefit.

Her general health improved, the sugar becoming less, but the eyes got steadily worse. The opacity in the vitreous of the left eye became denser, masses forming which appeared to contain cholesterin. The tension became increased and the sight by September had failed completely. The pupil was then noted as dilated and the iris "curiously vascular." No eserine had been used before these vessels appeared on the iris.

Her condition when I saw her in June, 1910, was as follows: The left eye had no P.L.; the pupil was circular, dilated and inactive. On the surface of the iris in the lower and inner part, for about a quarter of its extent, was a large-meshed network of new blood-vessels. They did not run radially from the ciliary margin but formed an irregular plexus. Large floating opacities with sparkling crystals could be seen in the vitreous. The optic disc, deeply cupped, was just visible. The tension was + 2.

In the right eye there were numerous posterior synechiæ, rendering the outline of the pupil very irregular. No new vessels were seen on the surface of the iris. There were numerous vitreous opacities. The tension was full; V. $= \frac{3}{12}$. Field of vision, tested with the hand, very restricted.

In association with the formation of these new vessels on the surface of the iris there is sometimes a thickening of its surface endothelium, so that the vessels seem to lie in an endothelial membrane. This is shown in the sections of the eye of which the following is the history:

Mary Ann M—, æt. 69 years, first seen on December 24th, 1889. The sight of the left eye had become foggy three days previously. Ophthalmoscopical examination showed "hæmorrhagic retinitis," with marked swelling of the optic disc = 2 D. The vision of the right eye was $= \frac{6}{9}$, and it showed no fundus changes. Urine: sp. gr. 1010, no albumen, no sugar. In the following February the left eye became glaucomatous, and eserine was prescribed. Ten days later the tension was still increased, the eye painful, and a few posterior synechia were seen at the lower part of the pupil. Atropine and cocaine oint-

PLATE X.

Illustrates Mr. E. Treacher Collins's paper on Fibrous Tissue Formation in Connection with the Fœtal Vascular System and Visible Vessels on the Surface of the Iris (p. 173).

Fig. 1.—Shows a microscopical section of the iris of the case recorded on p. 183. On its surface is shown a thickened endothelial membrane, in which a number of new-formed vessels are cut transversely.

Fig. 2.—Shows a portion of same iris more highly magnified. In it the arrangement of the vessels in the endothelial membrane is more clearly defined.

Fig. 1.

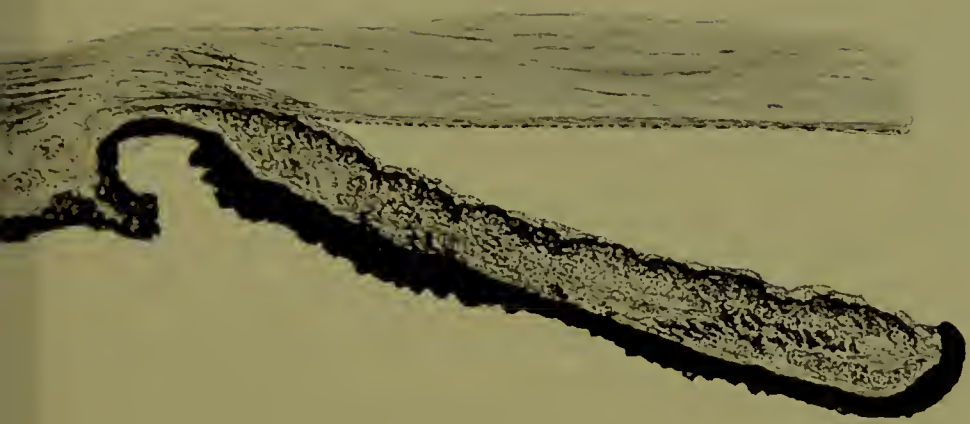
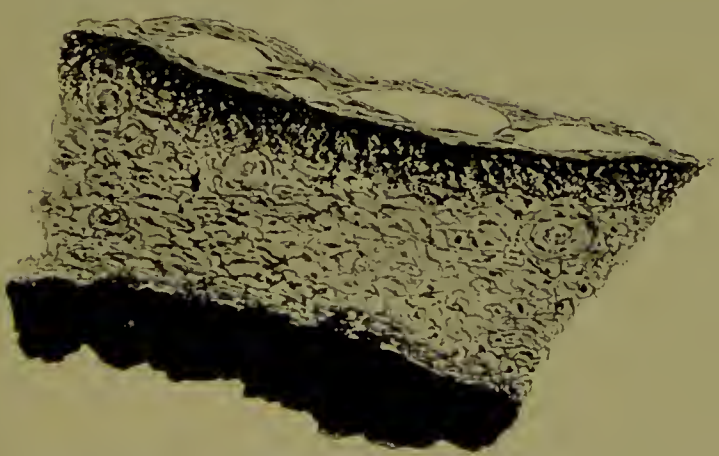


Fig. 2.



ment was then ordered. The sight became completely destroyed, the pupil widely dilated and the tension + 3, and it was excised on March 3rd, 1900.

The pathological examination of the eye showed the characteristic appearance of glaucoma secondary to thrombosis of the central retinal vein.

Microscopical examination of sections through the anterior part of the eye show the angle of the anterior chamber on one side to be closed by apposition of the root of the iris to the posterior surface of the cornea. On the other side the angle of the chamber is narrowed, but there is no contact of iris and cornea.

On both sides of the section the iris appears to be of normal thickness. There is no apparent atrophy of the root even where it is in contact with the cornea. There is no inflammatory exudation into its tissue, and no adhesions are seen between it and the lens capsule.

On the side on which the angle is closed the pigment epithelium turns round the pupillary margin, and is continued for a short distance on the anterior surface of the iris. The sphincter muscle is also tilted forwards at the pupillary border. On the opposite side the pigment epithelium terminates at its normal position, and there is no tilting forwards of sphincter muscle.

On the anterior surface of the iris on both sides of the section there is thickening of the endothelium. On the side on which the angle is closed there are in this thickened endothelium numerous thin-walled vessels, varying in size and cut mostly transversely (Pl. X, figs. 1 and 2). Most of them appear empty, but one is seen to contain a few red blood-corpuscles. On the side where the angle is open there is thickening of the surface endothelium throughout the whole length of the iris, but only one or two vessels are seen in it near the pupillary border.

The suggestion which I have to make as a possible explanation of the formation of these vessels on the surface of the iris is—that in certain cases of intra-ocular venous congestion some persistent tracks of the vessels of the

iridic portion of the fœtal lamina irido-pupillaris may become opened up and again capable of carrying blood.

These new vessels are situated in the position in which in fœtal life a plexus of vessels does exist, and are certainly not part of the normal structure of the adult iris.

Their arrangement in the form of a large-meshed network is the same as that of the vessels in the fœtal lamina irido-pupillaris. That they should be met with on only one portion of the surface of the iris, and that their distribution should be different in different cases, may be accounted for by variations in the extent to which portions of the fœtal membrane may have persisted on the surface of the iris.

The opening up of the old tracks of vessels would, I suggest, be analogous to recurrence of vascularity in the cornea, either after the subsidence of interstitial keratitis, or pannus, as the result of some fresh trivial lesion, such as an abrasion.

I am unable to suggest any reason why these new vessels should more frequently make their appearance in cases of increased tension secondary to thrombosis of the central retinal vein than in other forms of glaucoma.

References.

(1) Salzmann, M.—*The Anatomy and Histology of the Human Eyeball.* Trans. by E. V. L. Brown, 1912, p. 199.

(2) Mawas and Magitot.—*Travaux de la Fondation Ophtalmologique Adolphe de Rothschild,* 1902, p. 123.

(3) Hess, C.—*Archiv f. Ophth.,* Bd. xxxvi, Abt. III, p. 147.

(4) Coats, G.—"A Case of Microphthalmos, with Remarks," *The Ophthalmoscope,* October, 1910.

(5) Stephenson, S.—*Trans. Ophth. Soc. U.K.,* xxviii, 1908, p. 212, pl. xiii, fig. 3.

(6) Gunn, Marcus.—*Ibid.,* ix, 1889, p. 166, pl. ii, figs. 7 and 8.

PLATE XII.

Fig. 2 illustrates Mr. E. Treacher Collins's paper on Fibrous Tissue Formation in Connection with the Fœtal Vascular System and Visible Vessels on the Surface of the Iris (p. 173).

The arrangement of the blood-vessels on the surface of the iris in the case described on p. 180 is shown.

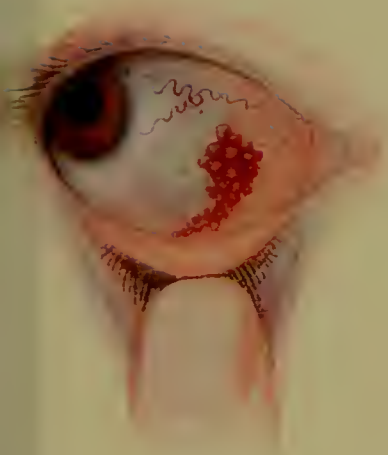


Fig. 1.

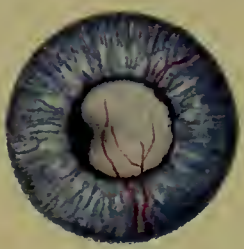


Fig. 2.

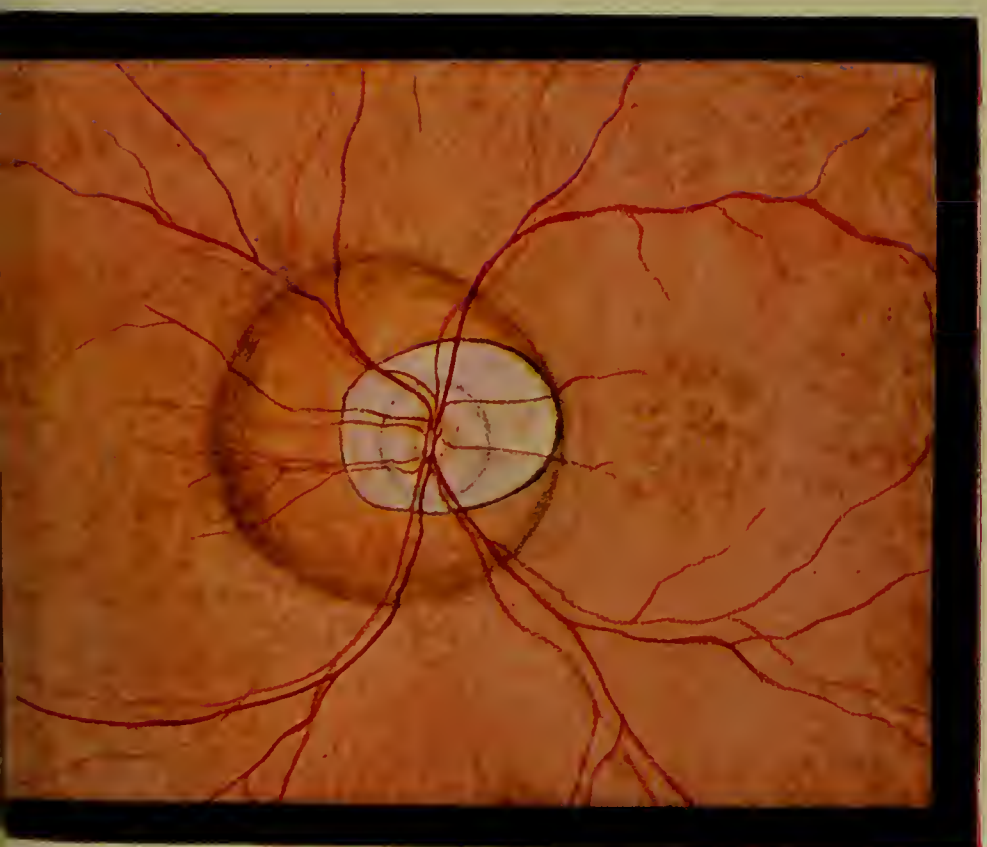


Fig. 3.

N. H. B. del. ad nat.

Adlard & Son, Impr.

(7) Greeff, R.—*Die pathologische Anatomie des Auges*, p. 223.

(8) Greeves, R. A.—*Roy. Lond. Ophth. Hosp. Reps.*, xviii, pt. iii, 1912, p. 313.

(9) Spicer, W. T. Holmes.—*Trans. Ophth. Soc. U.K.*, xxii, 1902, p. 306.

ADLARD AND SON, IMPR., LONDON AND DORKING.